(FILE 'HOME' ENTERED AT 14:44:52 ON 16 MAY 2003)

FILE 'CAPLUS' ENTERED AT 14:45:19 ON 16 MAY 2003
L1 421 S (VIRTUAL OR (IN SILICO)) (3W) SCREEN?
L2 179 S L1 AND LIBRARY
L3 11 S L2 AND FRAGMENT
L4 12 S L2 AND FRAGMENT?

=> d bib,abs 4,6,8

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2002:451675 CAPLUS
DN 137:345419
TI **Fragment** analysis in small molecule discovery
AU Merlot, Cedric; Domine, Daniel; Church, Dennis J.
CS Scientific Computing Department, Serono Pharmaceutical Research Institute, Geneva, Switz.
SO Current Opinion in Drug Discovery & Development (2002), 5(3), 391-399
CODEN: CODDFF; ISSN: 1367-6733
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review. Cheminformatics is playing an ever-increasing role in small mol. drug discovery. The widespread use of high-throughput screening (HTS) and combinatorial chem. techniques has led to the generation of large amts. of pharmacol. data which, in turn, has catalyzed the development of computational methods designed to reduce the time and cost in identifying mols. suitable for pharmaceutical development. This review focuses on recent advances in the field of substructure anal., an increasingly popular data mining technique with applications at many levels of the discovery process, including HTS, compd. **library** design, **virtual screening**, and the prediction of biol. activity.
RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2001:199843 CAPLUS
TI **Virtual** high-throughput **screening** of large datasets using TAE/RECON descriptors
AU Sukumar, Nagamani; Breneman, Curt M.; Katt, William P.
CS Department of Chemistry, Rensselaer Polytechnic Institute, Troy, NY, 12180, USA
SO Abstracts of Papers - American Chemical Society (2001), 221st, COMP-057
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB Recent developments using the method of Transferable Atom Equiv. (TAE) reconstruction will be discussed, including Wavelet Coeff. Desciptors (WCDs) and the evolution of automated atom type generation tools and automated lead testing algorithms. The TAE method, based on the Theory of Atoms in Mols., is an algorithm for the rapid reconstruction of mol. charge densities and charge-d.-based electronic properties of mols. using at. charge d. **fragments** precomputed from ab initio wavefunctions. The RECON algorithm inputs mol. geometries for a single mol. or an entire pharmaceutical database, dets. atom types and environments, assigns the closest match from a **library** of atom types, and combines the densities of the at. **fragments** to compute a large set of new and traditional QSAR descriptors. The TAE **library** contains information describing topol. features of the at. charge d. and at. charge d.-based descriptors, allowing for rapid retrieval of the **fragments** and mol. assembly. QSPR and QSER

indexes for individual proteins or large databases can be computed within seconds. We expect this emerging technol. to become a valuable tool in the rational design of target mols. having specific desired properties.

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2000:807156 CAPLUS
DN 134:95130
TI Development and screening of a polyketide virtual **library** for drug leads against a motilide pharmacophore
AU Siani, M. A.; Skillman, A. G.; Carreras, C. W.; Ashley, G.; Kuntz, I. D.; Santi, D. V.
CS Kosan Biosciences, Hayward, CA, USA
SO Journal of Molecular Graphics & Modelling (2000), 18(4/5), 497-511
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Science Inc.
DT Journal
LA English
AB A virtual **library** of macrocyclic polyketide mols. was generated and screened to identify novel, conformationally constrained potential motilin receptor agonists ("motilides"). A motilide pharmacophore model was generated from the potent 6,9-enol ether erythromycin and known derivs. from the literature. The pharmacophore for each mol. conformation was a point in a distance-vol. space based on presentation of the putative binding moieties. Two methods, one **fragment** based method and the other reaction based, were explored for constructing the polyketide virtual **library**. First, a virtual **library** was assembled from monomeric **fragments** using the CHORTLES language. Second, the virtual **library** was assembled by the in silico application of all possible polyketide synthase enzyme reactions to generate the product **library**. Each **library** was converted to low-energy 3D conformations by distance geometry and std. minimization methods. The distance-vol. metric was calcd. for low-energy conformations of the members of the **virtual** polyketide **library** and **screened** against the enol ether pharmacophore. The goal was to identify novel macrocycles that satisfy the pharmacophore. We identified three conformationally constrained, novel polyketide series that have low-energy conformations satisfying the distance-vol. constraints of the motilide pharmacophore.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT